REMARKS

Claims 1-18 and 21-39 are pending. Applicants elect with traverse Group I (claims 1-8 and 33-37) for examination on the merits. With regard to the requirement for an election of *Lactobacillus* species, (a) *Lactobacillus acidophilus* is elected. Claims 1-8 and 33-37 read on the elected *Lactobacillus* species (i.e., *Lactobacillus acidophilus*). Applicants reserve the right to prosecute non-elected subject matter in a further patent application.

Claim 1 is amended to recite that the modified protein is able to crystallize. This finds support on page 5, line 29, and page 6, last paragraph, of the specification. Claim 3(e) is amended to recite a maximum size of 300 kDa for the modified protein, which finds support on page 5, line 28, of the specification. Claim 4 is amended to recite that the crystallization or N-terminal domain is predominantly basic or hydrophobic, and the C-terminal domain is predominantly hydrophilic. This finds support on page 3, lines 31-32, and page 4, lines 12-13 (for the crystallization or N-terminal domain); and page 4, lines 2-3 and 18-19 (the C-terminal domain is the cell wall anchor), in combination with page 4, lines 25-28, of the specification.

Claim 9 is amended to depend from claim 1. A disclaimer is deleted from claim 15. Support for this amendment can be found on page 11 in the first full paragraph of the specification, where it is recited that the modified bacterium is preferably other than *L. casei* or *Bacillus*.

Claims 15 and 21 are amended to refer to the modified surface layer protein of claim 1. Claims 19-20 are deleted without prejudice or disclaimer. Claims 21-23 refers only to modified, and not to heterologous S-layer proteins. Support for this amendment can be found on page 13 in the last paragraph of the specification. Claim 25 recites that the bacteria has GRAS (generally regarded as safe) status. This finds support on page 15, lines 1-2, of the specification.

New claim 33 is supported by page 5, line 30, and page 8, lines 5-6, of the specification and original claim 27. New claims 34-37 specify preferred residues of SEQ ID NO:2 (which is the S-layer protein of *L. acidophilus*) at which a heterologous polypeptide can be inserted if the modified protein is to be able to crystallize. This finds support

in the paragraph bridging pages 6 and 7, and the first line on page 21 (which refers to SEQ ID NO:2), and in the Examples, in particular the last paragraph on page 41 and the last paragraph on page 44, of the specification. New claims 38 is directed to a process for using the elected product. It finds support on page 21, lines 10-20, of the specification. New claim 39 is directed to a process for making the elected product. It finds support on page 40, lines 4-7, of the specification.

Notwithstanding the above election, reconsideration of the restriction requirement is requested because examination of all pending claims would not constitute a serious burden. Therefore, the claims of Groups II to X should be examined in the same application. In particular, claims directed to bacteria and other products comprised of the bacterial surface layer proteins claimed in the elected Group I are combinations that should be examined in this application. With respect to the second restriction to a *Lactobacillus* species, it is noted that the pending claims are generic for *Lactobacillus acidophilus* and, thus, all *Lactobacillus* species should be examined for the generic claims.

In the alternative, Applicants disagree with the allegation in the Action that the pending claims lack unity of invention, and therefore belong to different groups of inventions. Traversal is based on the pending claims being so linked to form a single general inventive concept under PCT Rule 13.1. Blaser et al. (WO 98/33386) does not show a lack of novelty for the claimed invention or unity of invention. The present claims relate to a modified bacterial surface layer (S-layer) protein, the modification comprising the internal insertion of a heterologous polypeptide, wherein said modified protein is able to crystallize. The claimed subject matter is not anticipated by Blaser et al. Rather than disclosing the internal insertion of a heterologous polypeptide, Blaser et al. disclose the replacement of an internal fragment of SapA (the S-layer protein of *C. fetus*) by foreign sequences, such as HIV sequences. The insertion of a polypeptide is distinct from the replacement of residues as disclosed by Blaser et al. The hybrid S-proteins described by Blaser et al. lack a substantial fraction of the S-protein, in comparison to the modified S-layer proteins of the present invention. This renders them unable to crystallize. Accordingly, the pending claims are not anticipated by Blaser et al. and , therefore, Applicants request that the pending claims be examined together in this application.

Joinder of at least the claims belonging to Groups II, V and VI is appropriate in view of the present amendments. For example, claim 9 refers to a fragment of a protein according to claim 1. Thus, Applicants submit Groups I and II should be rejoined. Moreover, claims 15-20 (Group V) and claims 21-24 (Group VI) refer to an S-layer protein according to claim 1. Thus, Applicants submit Groups I and V-VI should be rejoined.

Furthermore, under the Commissioner's Notice of March 26, 1996 (1184 OG 86) implementing the Federal Circuit's decisions of *In re Ochiai*, 37 USPQ2d 1127 (1995) and *In re Brouwer*, 37 USPQ2d 1663 (1996), Applicants request rejoinder of process claims upon an indication that a product claim is allowable.

Applicants earnestly solicit an early and favorable examination on the merits. The Examiner is invited to contact the undersigned if any further information is required.

Respectfully submitted,

NIXON & VANDERHYE P.C.

By: _____

Gary R. Tanigawa
Reg. No. 43,180

901 North Glebe Road, 11th Floor
Arlington, VA 22203-1808
Telephone: (703) 816-4000
Facsimile: (703) 816-4100